REMARKS/ARGUMENTS

A. Status of the Claims

Claims 28 and 39 are amended, claims 45-46 are cancelled, and claims 47-49 are added. Support for these amendments and new claims can be found throughout the specification and claims as originally filed. No new matter has been added by this amendment. Therefore, claims 22-24, 28-40, 42-43, and 47-49 are currently pending.

B. The Written Description and Indefiniteness Rejections are Overcome

Claims 28, 39, 45 and 46 are rejected under 35 U.S.C. § 112 for lack of written description and indefiniteness. In view of the fact that claims 45 and 46 are canceled, the rejections as to these claims are moot. As for claim 28, it is alleged that the polysulfide prepolymer of claim 28 lacks written description "because the lower end of the average molecular weight range cannot be obtained even when the values of x and y are 1 or less." Action at page 2. Nothing is said to the weight range in claim 39 (*i.e.*, 650 to 1350 g mol^{-1}).

Applicants believe that there is no dispute that the specification provides ample support and clarity for claim 39, which now depends from new claim 48. Therefore, the rejection of this claim as well as claim 48 are believed to be moot at this time.

Although Applicants disagree with the rejections to claim 28, Applicants have revised this claim in an effort to further the prosecution of this case. Claim 28 now recites the molecular weight of the polysulfide prepolymer as being "not more than 3000 g mol^{-1}. Non-limiting support can be found at page 4 of the specification (identifying a prepolymer that does not exceed a molecular weight of 3000 g mol^{-1}). Applicants believe that this claim amendment renders the current written description and indefiniteness rejections moot.

However, in an effort to be as complete as possible, Applicants also provide detailed explanations in the following subsections that describe the scope of claim 28, illustrate written support for this claim, and confirm that this claim is indeed definite.

1. Scope of Claim 28

Applicants note that it has not sought protection for all polysulfides represented by formula (1a):

$$HS-\left[CH(CH_3)CH_2-S\right]_x-\left[CH_2CH_2S\right]_y-H$$

Rather, the scope of this claim is directed to polysulfides of formula (1a) that <u>**also**</u> meet the following conditions:

(i) the polysulfide is a prepolymer; and

(ii) the number average molecular weight of the polysulfide is not more than 3000 g mol^{-1}.

See claim 28. It is important to note that the integers x and y must be chosen such that the above two claimed elements are satisfied. Stated another way, claim 28 is not generically directed to prepolymers that have molecular weights of the specified values. Rather, the molecular weight limitations must also be read in the context of the entire claim. *See* MPEP § 2163 [II](A) (1) ("For Each Claim, Determine What the Claim as a Whole Covers").

2. Claim 28 Satisfies the Written Description Requirement

As noted in the above section, Applicants are not seeking protection for all possible compounds that can be created from generic formula (1a). Rather this formula (and integers x and y) are limited to compounds that are both (1) polysulfides, (2) prepolymers, and (3) have a molecular weight of not more than 3000 g mol^{-1}. There should be no dispute that the

specification provides ample written support for compounds that have formula (1a) and that are both polysulfides and prepolymers having a molecular weight of not more than 3000g mol^{-1}.

The argument that "applicants have failed to explain how the low molecular weight prepolymers, as claimed, can exist" (Action at page 3) is incorrect for at least two reasons. First, and as stated above, the claim 28 does not encompass all compound of formula (1a) that have molecular weights of not more than 3000g mol^{-1}. Rather, the x and y integers are chosen in a manner that leads to a compound of formula (1a) that has a molecular weight of not more than 3000g mol^{-1} and that is a polysulfide prepolymer. Stated another way, the "low molecular weight prepolymers" that the Examiner has an issue with are not covered by the claims because they are not polysulfide and/or prepolymers.

3. Claim 28 Is Definite

It is well-settled that "[t]he primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent." MPEP § 2173. There can be no dispute that a person of ordinary skill in the art would be able to identify prepolymers that fall within the scope of claim 28 as well as those that fall outside the scope of these claims. In fact, section 1 above provides an explanation of the scope of coverage for claim 28. This is sufficient to provide the notice function of § 112, second paragraph. *See* MPEP § 2173.02 ("In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent.").

4. New Claim 49 Satisfies the Written Description Requirement and Is Definite

New claim 49 concerns (α,ω)-diiso(thio)cyanate polysulfide prepolymer that has a number average molecular weight of not more than 3000 g mol^{-1}. This claim satisfies the written description and definiteness requirements of 35 U.S.C. § 112, first and second paragraphs, for at least the same reasons discussed above. The "not more than 3000 g mol^{-1}" limitation simply excludes molecular weights that are higher than 3000. Applicants note that claim 49 does not encompass all (α,ω)-diiso(thio)cyanates that have molecular weights of not more than 3000 g mol^{-1} but only those that are both (1) polysulfides and (2) prepolymers.

5. Conclusions Regarding the Written Description and Indefiniteness Rejections

When the molecular weights range limitations in claims 28 and 49 are read in the context of the entire claim, it is clear that the claims are supported by the specification and are definite. Again, only those polysulfide prepolymers that satisfy all the limitations in claims 28 and 49 are encompassed by the current claims. For at least these reasons, Applicants request that the rejections under 35 U.S.C. § 112 first and second paragraphs, be withdrawn.

C. The Anticipation Rejections Are Overcome

The Examiner presents two anticipation rejections under 35 U.S.C. § 102(a). In the first rejection, claims 22-24, 28-30, 33-35, 38, and 40, 42, 45 and 46 are allegedly anticipated by WO 01/36507. In the second rejection, claims 22-24, 28-30, 33-35, 38, and 40, 42, 43, 45 and 46 are allegedly anticipated by WO 01/36508. The two references are collectively referred to as the '507 and '508 Publications, respectively. In an effort to maintain the current rejections in view of the arguments submitted in Applicants' response of August 9, 2007, the examiner appears to argue that the '507 and '508 Publications disclose oligomers that do not necessarily contain disulfide groups. Action at pages 4-5.

Applicants disagree.[1,2] The following analysis of the '507 Publication is provided to explain why the Examiner's current position is factually and legally incorrect.

1. The Oligomers Disclosed in the '507 Publication Necessarily Have Disulfide Linkages

The '507 Publication discloses several oligomers on page 7, line 23, to page 9, line 30 and in claims 7 and 8. A critical analysis of these passages confirms that the oligomers necessarily have disulfide linkages (-S-S-). To begin, the '507 Publication explains at page 7 that the polythiol monomer can also include co-product oligomeric species and residual starting materials used during the synthesis of said polythiol monomer. Only oligomeric co-products are envisaged, and not any category of oligomer.

Indeed, according to this reference, polythiol monomers are obtained by esterification of a thiol functional carboxylic acid with a thiol functional alcohol, and co-products may arise from oxidative coupling of thiols during washing of the reaction mixture with excess base. It is well-known that oxidatively coupling thiols necessarily gives rise to disulfide compounds. Attached as Appendix A is a 2004 publication from Kirihara *et al.*, *Chem. Pharm. Bull.* 52(5) 625-627 (2004), confirming this. Although the '507 Publication states that "[s]uch an oxidative coupling **can result** in the formation of oligomeric polythiol species having disulfide linkages," there is no other possibility than to form a disulfide linkage. Indeed, it is a "chemical" necessity. *See* Appendix A. Oxidative coupling of thiols cannot lead to a compound which does not contain a disulfide group. Otherwise, the thiol group would not be oxidized. Therefore, the possibility expressed by the language "can" is not related to the presence or absence of disulfide linkages.

[1] Applicant also incorporates the arguments and evidence made in the previous responses into this response.
[2] The disclosures in the '507 and '508 Publications are substantially identical with respect to the anticipation rejections. In an effort to be efficient, all of the arguments focus on the '507 Publication. However, all of the arguments made against the '507 Publication equally apply to the '508 Publication.

For at least the above reasons, it is submitted that the analysis of the cited references at pages 4-5 of the Office Action is incorrect. Besides, the examiner has not meet his burden demonstrated that oxidative coupling of thiols provides compounds that anticipate applicants' claimed invention, *i.e.*, a polythiol oligomer free of disulfide linkage. *See In re Sun*, 31 U.S.P.Q.2d 1451,1453 (Fed. Cir. 1993) (explaining the initial burden of proving anticipation is on the Examiner).

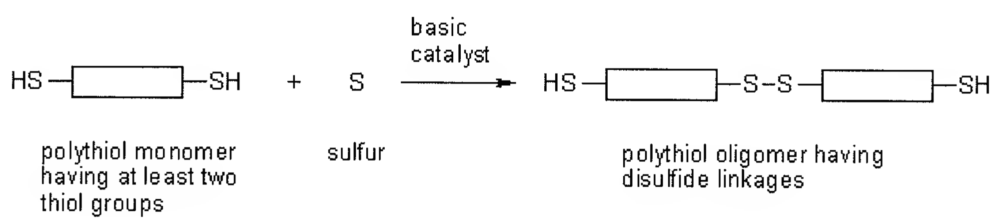
2. The "may be" Language in the '507 Publication Does Not Disclose Polysulfide Prepolymers Being Free From Disulfide Linkages

The current anticipation rejections appear to be based, in part, on the following disclosure in the '507 Publication:

> The polythiol monomer used to prepare the polycyanate reactant **may be** a polythiol oligomer having disulfide linkages, which is prepared from the reaction of a polythiol monomer having at least two thiol groups and sulfur in the presence of a basic catalyst.

Id. at page 8, line 35 (emphasis added).

For purposes of clarity and to resolve the current anticipation rejections, Applicants must stress that the phrase "may be" in the above passage explains that the polythiol monomer may be a polythiol oligomer comprising an S-S bond, prepared according to the following scheme:



This means that the polythiol monomer may be an oligomer bearing a disulfide group, and does not mean that the polythiol monomer may be an oligomer free of a disulfide group. "May be" expresses a possibility related to the phrase "polythiol monomer," not the phrase

"disulfide linkages." Consequently, such language does not confirm the optional presence of disulfide groups.

Further, it is clear that the disclosed oligomers in the '507 Publication all bear at least one disulfide linkage, for at least the following three reasons:

(a) Although it is written that "**oligomers** of general formula I which can be described by general formula Ia" (page 8, lines 10-12) (emphasis added), it is immediately explained that "general structure Ia is meant to represent **all possible oligomers** that can form from general structure I" (page 8, lines 19-20) (emphasis added). Seeing that compounds of formula Ia include at least one disulfide linkage, it can be concluded that the '507 Publication does not contemplate oligomers other than those having a disulfide linkage.

(b) Oligomers of formula II also bear at least one disulfide linkage.

(c) Oligomers are called "polythiol **oligomer** having disulfide linkages" several times (*see* page 8, lines 21-22; page 9, lines 10-11; page 9, lines 17-18; page 9, lines 22-23) (emphasis added).

As a conclusion, there is no disclosure that establishes that any disclosed oligomeric compound is free of disulfide linkage. Rather, the cited art only describes or suggests oligomers bearing at least one disulfide linkage. Indeed, the presence of this disulfide group is inherent to their synthetic pathway.

3. Applicants Request the Examiner to Identify One Polysulfide Prepolymer Being Free of Disulfide Linkages

Given the above arguments and explanations, Applicants believe that the cited references fail to disclose Applicants' claimed polysulfide prepolymer being free of disulfide linkages. To make the record complete for appellate purposes, Applicants request the Examiner to point to **any** oligomer in the cited references that meets Applicants' claimed polysulfide prepolymer being free of disulfide linkages.

Again, this is a burden that the Examiner's bears. *See In re Sun*, 31 U.S.P.Q.2d at 1453 (Fed. Cir. 1993). It is not sufficient for the Examiner to simply state that "one would

immediately envisage…" the claimed polysulfide prepolymer to support the anticipation rejection (Action at page 5). Rather, "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *See In re Bond*, 910 F.2d 831, 832 (Fed. Cir. 1990).

4. Conclusion Regarding the Anticipation Rejections

The '507 and '508 Publications explain in their respective disclosures that polymerization of polythiol monomers necessary results in oligomers having at least one disulfide linkage. The disulfide linkage is the result of oxidative coupling of thiol groups between the monomers. There is no disclosure that establishes that any disclosed oligomeric compound is free of disulfide linkage. In fact, the presence of this group is inherent to the '507 and '508 Publications synthetic pathway.

The presence of the disulfide linkage in the '507 and '508 Publication oligomers is in contrast to Applicants' claimed "(α, ω)-diiso(thio)cyanate polysulfide prepolymer, which is "free from disulfide (-S-S-) linkage." Therefore, the cited references fail to disclose every element of the claimed invention, and the anticipation rejection should be withdrawn.

D. Conclusion

Applicants believe that the present document is a full and complete response to the Office Action mailed October 18, 2007. The present case is in condition for allowance and such favorable action is requested.

The Examiner is invited to contact the undersigned Attorney at (512) 536-3020 with any questions, comments or suggestions relating to the referenced patent application.

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APPENDIX A
(Kirihara *et al.*, 2004)

Aerobic Oxidation of Thiols to Disulfides Catalyzed by Trichlorooxyvanadium

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Thiols were converted into disulfide by the aerobic oxidation catalyzed by trichlorooxyvanadium in the presence of molecular sieves 3A.

Key words thiol; disulfide; oxidative coupling; aerobic oxidation

Oxidative coupling of thiols to disulfides is of interest from both a synthetic and a biological point of view, because disulfides are useful reagent in organic synthesis[1—3] and essential moieties of biologically active compounds for peptide and protein stabilization.[4] Thiols can be easily over-oxidized, and therefore, several selective methods of converting thiols into disulfides have been developed. For example, iodine/hydrogen iodide,[5] bromine,[6,7] potassium permanganate/copper(II) sulfate,[8] hydrogen peroxide in trifluoroethanol,[9] and dimethyl sulfoxide[10—12] are used for this purpose. Most of the existing methods suffer from drawbacks such as the use of stoichiometric amounts of reagents that generate undesirable waste materials. To overcome these drawbacks, catalytic oxidation using oxygen as a co-oxidant has been developed by several groups.[13—18]

We have been investigating the aerobic oxidation of organic compounds catalyzed by higher valent vanadium compounds.[19—36] Stoichiometric higher valent vanadium compounds are known to oxidize thiols to produce disulfides,[37,38] and a catalytic amount of vanadyl acetylacetonate is also known to cause the oxidative coupling of thiols in the presence of *t*-butylhydroperoxide.[39] However, there have been no reports about the aerobic oxidative coupling of thiols catalyzed by vanadium compounds. We now describe a novel aerobic oxidative coupling of thiols to disulfides using trichlorooxyvanadium ($VOCl_3$) as a catalyst (Chart 1).

$$\text{R—SH} \xrightarrow{\text{cat. } VOCl_3,\ O_2} \text{1/2 RS—SR}$$

Chart 1

We first examined the oxidation of didodecylthiol as a model substrate with 0.4 eq of $VOCl_3$ under an oxygen atmosphere in several kinds of solvents (Table 1). The reaction efficiently proceeded in aprotic polar solvents such as ethyl acetate (run 3) and acetonitrile to provide didodecyl disulfide[40] (run 4).

Table 1

$$CH_3(CH_2)_{11}\text{–}SH \xrightarrow[\text{1/2 } CH_3(CH_2)_{11}S\text{–}S(CH_2)_{11}CH_3]{0.4\text{ eq } VOCl_3,\ O_2,\ \text{solvent}}$$

Run	Solvent	Time	Yield
1	C_6H_6	5 d	52%
2	CH_2Cl_2	44 h	51%
3	AcOEt	22 h	93%
4	CH_3CN	26 h	82%
5	CH_3OH	51 h	Trace

We then investigated the reaction of butanthiol with several higher valent vanadium catalysts in ethyl acetate under an oxygen atmosphere (Table 2). Dibutyl disulfide[41] was quantitatively obtained in the case of $VOCl_3$ (a pentavalent vanadium) (run 1). On the other hand, tetravalent vanadiums {vanadyl chloride ($VOCl_2$) (run 2) and vanadyl acetylacetonate [$VO(acac)_2$] (run 3)} did not have sufficient catalytic activity.

Table 2

$$n\text{-Bu–SH} \xrightarrow[\text{AcOEt}]{0.4\text{ eq catalyst, } O_2} \text{1/2 } n\text{-BuS–S}n\text{-Bu}$$

Run	Catalyst	Time	Yield
1	$VOCl_3$	3 h	Quant
2	$VOCl_2$	41 h	13%
3	$VO(acac)_2$	41 h	28%

Although the oxidation of butanthiol smoothly proceeded to afford the disulfide, over 0.4 eq of $VOCl_3$ was required to complete the reaction (Table 3).

Table 3

$$n\text{-Bu–SH} \xrightarrow{\text{catalyst, } O_2,\ \text{AcOEt}} \text{1/2 } n\text{-BuS–S}n\text{-Bu}$$

Run	Catalyst	Time	Yield
1	0.4 eq $VOCl_3$	3 h	Quant
2	0.3 eq $VOCl_3$	28 h	66%
3	0.2 eq $VOCl_3$	24 h	30%

We assumed that water produced from the oxidative coupling of a thiol deactivated the vanadium catalyst. Therefore, molecular sieves 3A were added to the reaction mixture to remove the water.[42,43] In the presence of the molecular sieves 3A, only 0.05 eq $VOCl_3$ was enough to complete the reaction (Chart 2).

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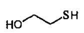
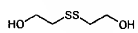
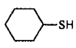
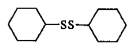
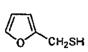
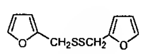
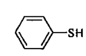
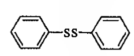
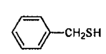
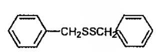
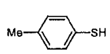
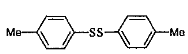
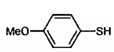
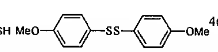
$$n\text{-Bu SH} \xrightarrow[\text{molecular sieves 3A, rt, 43 h}]{0.05\text{ eq } VOCl_3,\ O_2,\ \text{AcOEt}} 1/2\ n\text{-BuS—S}n\text{-Bu}$$

98%

Chart 2

Table 4

$$\text{RSH} \xrightarrow[\text{molecular sieves 3A, rt}]{0.05\text{ eq } VOCl_3,\ O_2,\ \text{AcOEt}} 1/2\ \text{RS–SR}$$

Entry	Thiol	Product[a]		Time (h)	Yield (%)
1	$CH_3(CH_2)_{11}SH$	$CH_3(CH_2)_{11}SS(CH_2)_{11}CH_3$	40	111 (22)[b]	88 (93)[b]
2	$CH_3(CH_2)_3SH$	$CH_3(CH_2)_3SS(CH_2)_3CH_3$	41	43 (3)[b]	98 (quant)[b]
3			44	1.5 (0.5)[b]	84 (75)[b]
4			13	41 (5)[b]	53[c] (93)[b]
5			45	109	80
6			13	52 (22)[b]	93 (99)[b]
7			16	74 (4)[b]	91 (99)[b]
8			46	20	96
9			46	66	98

a) The physical data of the products were consistent with those of references. *b*) 0.4 eq of $VOCl_3$ was used without molecular sieves 3A. *c*) Unidentified by-products were obtained.

This method is equally applicable for the oxidative coupling of several kinds of thiols (Table 4). In the parentheses, we also show the results of the reaction using 0.4 eq $VOCl_3$ without molecular sieves. Although the reaction rates were relatively slow, dislufides were efficiently obtained in most cases. As noted in the entry 3, 2-mercaptoethanol was oxidized much faster than in the other cases. The reason for this interesting phenomenon has not been clarified.

In conclusion, the $VOCl_3$-catalyzed aerobic oxidative coupling of thiols should be a good method to prepare disulfides.

Experimental

General Procedures Thiols and vanadium compounds were obtained from Wako Pure Chemical Industries, Kanto Kagaku, Nacalai Tesque, or Tokyo Kasei Kogyo without purification. Products were characterized by comparison of their physical data with those of known samples.

The Aerobic Oxidation of Thiols Catalyzed by Trichlorooxyvanadium in the Presence of Molecular Sieves 3A: General Procedures To a stirred mixture of thiol (4.0 mmol), molecular sieves 3A (1.0 g) and ethyl acetate (4.0 ml) was added $VOCl_3$ (35 mg, 0.2 mmol) under an oxygen atmosphere at room temperature. The reaction was monitored by thin layer chromatography and was continuously stirrered under the same conditions until the thiol disappeared. After the reaction was completed, a drop of saturated aqueous sodium bicarbonate was added and diluted with ethyl acetate (30 ml). The resulting mixture was filtered with Cerite and the filtrate was dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was purified by silica gel column chromatography (hexane–ethyl acetate as the eluents) to afford the pure products.

Acknowledgments This work was supported in part by the Regional Science Promotion Program of Japan Science and Technology Corporation. We would like to express our appreciation to Mr. Masao Yaso (Regional Science Promotion Program of Japan Science and Technology Corporation), for his helpful suggestions.

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